Applicants: David Baltimore et al.

Serial No.: CPA of 08/813,323 Filed : March 10, 1997

Page 3

REMARKS

Claims 3, 4 and 92 are pending in the above-identified application. By this Amendment applicants have canceled claims 3, 4 and 92 and added new claims 93 and 94. New claim 93 is supported by the application as originally filed, for example at page 8, lines 3-7; page 12, lines 13-14; Figure 1; and Figure 3, inter alia. New claim 94 is supported by the application as originally filed, for example at page 8, lines 3-7; page 12, lines 13-14; Figure 1; and Figure 3, inter alia. Applicants maintain that the amendments to the claims raise no issue of new matter and therefore request that the Amendment be entered into the application. After entry of this Amendment claims 93 and 94 will be pending.

In addition, applicants have corrected the Sequence Listing. Applicants inadvertently omitted the carboxy-terminal residue from SEQ ID NO:1 (Figure 1) in the Sequence Listing filed November 25, 1997 with the United States Patent and Trademark Office in connection with the above-identified application. Accordingly, applicants attach hereto a paper copy sequence Listing, a Computer Readable Form Sequence Listing and a Statement in Accordance with 1.821(f) as Exhibit B. Applicants maintain that the corrected Sequence Listing raises no issue of new matter.

Rejections Under 35 U.S.C. §112, First Paragraph

The Examiner stated that rejection under 35 U.S.C. §112, first paragraph of claims 3, 4, 92, pertaining to lack of a clear written description of an amino-terminal at amino acid 385, remains for reasons already of record in paper No. 24.

Applicants:

David Baltimore et al.

Serial No.:

CPA of 08/813,323 March 10, 1997

Filed Page 4

The Examiner stated that applicants assert that page 8, lines 3-5 of the specification disclose a portion of SEQ ID NO:1, which portion has as its amino-terminal boundary any one of amino acid residues from 324 to 415 of SEQ ID NO:1. The Examiner stated that applicants' arguments set forth in paper No.25 have been considered but are not deemed to be persuasive for the following reasons: page 8, lines 3-5 of the specification does not disclose a portion of SEQ ID NO:1, which portion has as its amino-terminal boundary any one of amino acid residues from 324 to 415 of SEQ ID NO:1. The Examiner stated that page 8, lines 3-5 of the specification only discloses a truncated CRAF1 by from about 323 to about 414 amino acid residues at the amino terminus, or a variant thereof capable of inhibiting CD-40 mediated cell activation.

In response, without conceding the correctness of the Examiner's position, applicants have canceled claims 3, 4, and 92 and added new claims 93 and 94. As noted above, new claims 93 and 94 are fully supported by the specification as originally filed.

Rejection Under 35 U.S.C. §102(b)

The Examiner stated that the rejection under 35 U.S.C. §102(b) of claims 3, 4, 92, pertaining to anticipation by Sato et al., remains for reasons already of record in paper No. 24.

The Examiner stated that applicants assert that the protein disclosed by Sato et al. does not have an amino-terminus between residues 324 and 385 of SEQ ID NO:1, and that the amino-terminus of the Sato protein occurs at residue 387. The Examiner stated that applicants' arguments set forth in paper No. 25 have been

Applicants: David Baltimore et al.

Serial No.: CPA of 08/813,323 Filed : March 10, 1997

Page 5

considered but are not deemed to be persuasive for the following reasons: The Examiner stated that the claims do not necessarily read on a protein having an amino-terminus between residues 324 and 385 of SEQ ID NO: 1, and, thus, applicants argue a limitation not in the claims.

In response, without conceding the correctness of the Examiner's position, applicants have canceled claims 3, 4, and 92, and added new claims 93 and 94. Applicants note that claim 93 is directed to a specific peptide having a sequence defined in the claim. This peptide differs from both of the human-derived peptides disclosed by Sato et al., one of 153 amino acids (full length CRAF-1) and the other of 181 amino acids (a fragment of CRAF-1), in that the claimed peptide is shorter in length (only 153 residues). Applicants assert, therefore, that claim 93 is not anticipated by Sato et al.

In addition, applicants' claim 94 recites a specific peptide having a sequence defined in the claim. This sequence is included within SEQ ID NO:1. Applicants note that SEQ ID NO:1 describes a peptide derived from a mouse. In contrast, Sato et al. disclose two humanderived peptides, one of 543 amino acids (full length CRAF-1) and the other of 181 amino acids (a fragment of CRAF-1). Applicants note that the specific peptides described in claim 94 contain residue differences with both the fragment and the full-length human sequences disclosed by Sato et al. For example, there is a threonine residue at position 390 in the claimed peptide, whereas both the Sato peptides have a methionine at their corresponding position (residue 366 by Sato's numbering). For example, there is a further difference at residue 373. with the claimed peptide

Applicants:

David Baltimore et al.

Serial No.:

CPA of 08/813,323 March 10, 1997

Filed Page 6

having an alanine at that position and both the Sato fragments having a valine (residue 349 by Sato's numbering). Thus, Sato et al. does not anticipate applicant's claimed invention.

In summary, in light of the remarks made hereinabove, applicants respectfully request that the Examiner reconsider and withdraw the various grounds of rejection set forth in the February 12, 2002 Final Office Action.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee, other than the \$55.00 fee for a one-month extension of time is deemed necessary in connection with the filing of this Amendment. If any such fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Honorable Commissioner for Patents and Trademarks, Washington, D.C. 20231, BOX AF

JAN Date Date

John P. White Reg! No. 28,678 0/2/12

Respectfully submitted,

John D. White
Registration No. 28,678
Attorney for Applicants
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, New York 10036
(212) 278-0400



COPY OF PAPERS ORIGINALLY FILED

SEQUENCE LISTING

<110> Baltimore, David
 Cheng, Genhong
 Ye, Zheng-Sheng
 Lederman, Seth
 Cleary, Aileen

<120> Truncated Craf-1 Inhibits CD40 Signalling

<130> 0575/50659

<140> US/ 08/813,323

<141> 1997-03-10

<160> 5

<170> PatentIn version 3.1

<210>

<211> 567

<212> PRT

<213> Mouse Sp.

<400> 1

Met Glu Ser Ser Lys Lys Met Asp Ala Ala Gly Thr Leu Gln Pro Asn
1 10 15

Pro Pro Leu Lys Leu Gln Pro Asp Arg Gly Ala Gly Ser Val Leu Val

Pro Glu Gln Gly Gly Tyr Lys Glu Lys Phe Val Lys Thr Val Glu Asp

Lys Tyr Lys Cys Glu Lys Cys Arg Leu Val Deu Cys Asn Pro Lys Gln
50 55 60

Thr Glu Cys Gly His Arg Phe Cys Glu Ser Cys Met Ala Ala Leu Leu 65 70 75 80

Ser Ser Ser Pro Lys Cys Thr Ala Cys Gln Glu Ser Ile Ile Lys
85 90 95

Asp Lys Val Phe Lys Asp Asn Cys Cys Lys Arg Glu Ile Leu Ala Leu
100 105

Gln Val Tyr Cys Arg Asn Glu Gly Arg Gly Cys Ala Glu Gln Leu Thr 115 120 125

Leu Gly His Leu Leu Val His Leu Lys Asn Glu Cys Gln Phe dlu Glu
130 135 140

Leu Pro Cys Leu Arg Ala Asp Cys Lys Glu Lys Val Leu Arg Lys Asp
145 150 155 460



Leu Arg Asp His Val Glu Lys Ala Cys Lys Tyr Arg Glu Ala Thr Cys
165 170 175

Ser His Cys Lys Ser Gln Val Pro Met Ile Lys Leu Gln Lys His Glu 180 185 190

Asp Thr Asp Cys Pro Cys Val Val Val Ser Cys Pro His Lys Cys Ser 195 200 205

Val Gln Thr Leu Leu Arg Ser Glu Leu Ser Ala His Leu Ser Glu Cys 210 220

Val Asn Ala Pro Ser Thr Cys Ser Phe Lys Arg Tyr Gly Cys Val Phe 225 230 235 240

Gln Gly Thr Asn Gln Gln Ile Lys Ala His Glu Ala Ser Ser Ala Val 245 250 255

Gln His Val Asn Leu Leu Lys Glu Tap Ser Asn Ser Leu Glu Lys Lys 260 265 270

Val Ser Leu Leu Gln Asn Glu Ser Val Glu Lys Asn Lys Ser Ile Gln
275 280 285

Ser Leu His Asn Gln Ile Cys Ser Phe Glu Ile Glu Ile Glu Arg Gln 290 295 300

Lys Glu Met Leu Arg Asn Asn Glu Ser Lys Ile\Leu His Leu Gln Arg 305 310 315

Val Ile Asp Ser Gln Ala Glu Lys Leu Lys Glu Leu Asp Lys Glu Ile 325 330 335

Arg Pro Phe Arg Gln Asn Trp Glu Glu Ala Asp Ser Met Lys Ser Ser 340 350

Val Glu Ser Leu Gln Asn Arg Val Thr Glu Leu Glu Ser Val Asp Lys 355 360 365

Ser Ala Gly Gln Ala Ala Arg Asn Thr Gly Leu Leu Glu Ser Gla Leu 370 380

Ser Arg His Asp Gln Thr Leu Ser Val His Asp Ile Arg Leu Ala Asp 385 390 395 400

Met Asp Leu Arg Phe Gln Val Leu Glu Thr Ala Ser Tyr Asn Gly Val 405 410 415

Leu Ile Trp Lys Ile Arg Asp Tyr Lys Arg Arg Lys Gln Glu Ala Val 420 425 430

Met Gly Lys Thr Leu Ser Leu Tyr Ser Gln Pro Phe Tyr Thr Gly Tyr
435
440
445

Phe Gly Tyr Lys Met Cys Ala Arg Val Tyr Leu Asn Gly Asp Gly Met 450 450 460

Gly Lys Gly Thr His Leu Ser Leu Phe Phe Val Ile Met Arg Gly Glu 465 470 475 480

Tyr Asp Ala Leu Leu Pro Trp Pro Phe Lys Gln Lys Val Thr Leu Met 485

Leu Met Asp Gln Gly Ser Ser Arg Arg His Leu Gly Asp Ala Phe Lys
500 505 510

Pro Asp Pro Asn Ser Ser Ser Phe Lys Lys Pro Thr Gly Glu Met Asn 515 520 525

Ile Ala Ser Gly Cys Pro Val Phe Val Ala Gln Thr Val Leu Glu Asn 530 535

Gly Thr Tyr Ile Lys Asp Asp Thr Ile Phe Ile Lys Val Ile Val Asp 545 550 555 560

Thr Ser Asp Leu Pro Asp Pro 565

<210> 2

<211> 568

<212> PRT

<213> Homo Sapiens

<400> 2

Met Glu Ser Ser Lys Lys Met Asp Ser Pro Gly Ala Leu Gln Thr Asn
1 10 15

Pro Pro Leu Lys Leu His Thr Asp Arg Ser Ala Gly Thr Pro Val Phe 20 25 30

Val Pro Glu Gln Gly Gly Tyr Lys Glu Lys Phe Val Lys Thr Val Glu 35 40 45

Asp Lys Tyr Lys Cys Glu Lys Cys His Leu Val Leu Cys Ser Pro Lys 50 55 60

J2/1

Gln Thr Gla Cys Gly His Arg Phe Cys Glu Ser Cys Met Ala Ala Leu 65 70 75 80

Leu Ser Ser Ser Pro Lys Cys Thr Ala Cys Gln Glu Ser Ile Val 85 90 95

Lys Asp Lys Val Phe Lys Asp Asn Cys Cys Lys Arg Glu Ile Leu Ala

Leu Gln Ile Tyr Cys Arg Asn Glu Ser Arg Gly Cys Ala Glu Gln Leu 115 120 125

Thr Leu Gly His Leu Leu Val His Leu Lys Asn Asp Cys His Phe Glu 130 135 140

Glu Leu Pro Cys Val Arg Pro Asp Cys Lys Glu Lys Val Leu Arg Lys
145 150 155 160

Asp Leu Arg Asp His Val Glu Lys Ala Cys Lys Tyr Arg Glu Ala Thr 165 170 175

Cys Ser His Cys Lys Ser Gln Val Pro Met Ile Ala Leu Gln Lys His 180 185 190

Glu Asp Thr Asp Cys Pro Cys Val Val Sar Cys Pro His Lys Cys 195 200 205

Ser Val Gln Thr Leu Leu Arg Ser Glu Leu Ser Ala His Leu Ser Glu 210 215 220

Cys Val Asn Ala Pro Ser Thr Cys Ser Phe Lys Arg Tyr Gly Cys Val 225 230 235 240

Phe Gln Gly Thr Asn Gln Gln Ile Lys Ala His Glu Ala Sèr Ser Ala 245 250 255

Val Gln His Val Asn Leu Leu Lys Glu Trp Ser Asn Ser Leu Glu Lys
260 265 270

Lys Val Ser Leu Leu Gln Asn Glu Ser Val Glu Lys Asn Lys Ser Leu 275 280 285

Gln Ser Leu His Asn Gln Ile Cys Ser Phe Glu Ile Glu Ile Glu Arg 290 295 · 300

Gln Lys Glu Met Leu Arg Asn Asn Glu Ser Lys Ile Leu His Leu Gln 305 310 315 320

Arg Val Ile Asp Ser Gln Ala Glu Lys Leu Lys Glu Leu Asp Lys Glu 325 330 335

Ile Arg Pro Rhe Arg Gln Asn Trp Glu Glu Ala Asp Ser Met Lys Ser 345 350

Ser Val Glu Ser Deu Gln Asn Arg Val Thr Glu Leu Glu Ser Val Asp 355 360 365

Lys Ser Ala Gly Gln Wal Ala Arg Asn Thr Gly Leu Leu Glu Ser Gln 370 380

Leu Ser Arg His Asp Gln Met Leu Ser Val His Asp Ile Arg Leu Ala 385 390 400

Asp Met Asp Leu Arg Phe Gln Val Leu Glu Thr Ala Ser Tyr Asn Gly
405 410 415

Val Leu Ile Trp Lys Ile Arg Asp Tyr Lys Arg Arg Lys Gln Glu Ala 420 425 430

Val Met Gly Lys Thr Leu Ser Leu Tyr Ser Gln Pro Phe Tyr Thr Gly
435 440 445

Tyr Phe Gly Tyr Lys Met Cys Ala Arg Val Tyr Leu Asn Gly Asp Gly 450 455

Met Gly Lys Gly Thr His Leu Ser Leu Phe Phe Val Ile Met Arg Gly
465 470 475 480

Glu Tyr Asp Ala Leu Leu Pro Trp Pro Phe Lys Gln Lys Val Thr Leu 485 490 495

Met Leu Met Asp Gln Gly Ser Ser Arg Arg His Leu Gly Asp Ala Phe 500 505

Lys Pro Asp Pro Asn Ser Ser Ser Phe Lys Lys Pro Thr Gly Glu Met 515 520 525

Asn Ile Ala Ser Gly Cys Pro Val Phe Val Ala Gln Thr Val Leu Gl $\dot{\chi}$ 530 535 540

Asn Gly Thr Tyr Ile Lys Asp Asp Thr Ile Phe Ile Lys Val Ile Val 545 550 555 560

Asp Thr Ser Asp Leu Pro Asp Pro 565

(m)

<210> 2359 Mouse Sp. <400> ggcggcggag gatgcgcgcgg gcgcctgagc cggccgaacg ggcggcctcg gggtacaggg 60 tececattae ttgaaggata agetteegae ggeteegaeg tetgtgtgga agetteteee 120 tecettetga gettetetag ackeettaca gegeaeggea cagaatttea gttteetaag 180 atggagtcaa gcaaaaagat ggatgctgct ggcacactgc agcctaaccc acccctaaag 240 300 ctgcagcctg atcgcggcgc agggtcoqtg ctcgtgccgg agcaaggagg ctacaaggag aagtttgtga agacggtgga agacaagtàc aagtgcgaga agtgccgcct ggtgctgtgc 360 aacccgaagc agaeggagtg tggccaccgg ttctgcgaga gctgcatggc.cgccctgctg. 420. agetecteca gtecaaaatg cacagegtge caagaaagea teateaaaga caaggtgttt 480 aaggataatt gctgcaagag agagattctg gcc&ttcagg tctactgtcg gaatgaaggc 540 600 agaggttgtg cggagcagct gactctggga catctgctgg tgcacctaaa aaatgaatgt cagtttgagg aacttccctg tctgcgtgcc gactgcaaag aaaaagtact gagaaaagac 660 ttgcgggatc acgtggaaaa ggcctgtaaa taccgcgagg ccacgtgcag tcactgcaag 720 780 agccaagtgc ccatgatcaa actgcagaaa catgaagaca kagattgtcc ctgtgtggtg gtatcctgcc ctcacaagtg cagcgttcag actcttctaa ggagtgagtt gagtgcacac 840 ttgtccgagt gtgtcaatgc ccccagcacc tgtagtttta agcgctatgg ctgcgttttt 900 cagggtacaa accagcagat caaggcccat gaggccagct ccgcggtaca gcacgtgaac 960 ctgctgaagg agtggagcaa ctccctggag aagaaggttt ccctgctgca gaatgaaagt 1020 gttgagaaaa acaagagcat ccaaagcctg cacaaccaga tctgcagctt tgagatcgag 1080 attgagaggc agaaggagat gctccgaaac aacgagtcca agatccttca &ctgcagcgg 1140 gtaatcgaca gccaagcaga gaaactgaaa gaactggaca aggagatccg tccttccgg 1200 cagaactggg aggaagcgga cagcatgaag agcagtgtgg agtccctcca gaadcgagtg 1260 actgagctgg agagcgtaga caaaagtgcg gggcaggcgg ctcgcaacac aggctkgctg 1320 1380 gagtcccagc tgagccggca tgaccagacg ttgagtgttc atgacatccg cttggccgac atggacctgc ggttccaggt cctcgagacc gccagctaca acggggtgct gatctggaag 1440 atccgtgact acaagcgccg gaagcaggag gccgtcatgg ggaagaccct gtctctctac 1500 agccagcctt tctacacagg ttattttggc tataagatgt gtgccagggt ctacctgaat 1560 ggggacggaa tggggaaagg gacacacttg tcgctgtttt ttgtcattat gcgtggagaa 1620 1680 tatgatgctc tgttgccatg gccgttcaag cagaaagtga cacttatgct gatggatcag gggtcctctc gccgtcatct gggagatgcg ttcaagcctg accccaacag cagcagcttc 1740

aagaaaccca ccggagagat gaatatcgcc tctggctgcc cagtctttgt cgcccaaact 1800 gttctagaga acgggacgta tattaaagat gatacaatct ttattaaggt catagtggat 1860 acctcggatc\tgcctgaccc ctgacaagaa agcagggcgg tggattcagc agaaggtaac 1920 tectetgggg gggtgageta gtgtetteae ggaggteete geeeteagaa aggaeettgt 1980 ggcgcagagg aaqcagccgg aggaggagaa ggaggtcgag tggctggcag gagagccaca 2040 tgtgaaaaca gaccccaacg gattttctaa taaactagcc acacccactc tgaaggatta 2100 2160 tttatccatc aacaagataa atactgctgt cagagaaggt tttcattttc attttaaaag atctagtatt aaggtgggaa catatatgct aaaaagaaac atgatttttc ttccttaact 2220 taaacaccaa aaagagaaca atgtggggg tagctggagt gtgtacagta cctcgagggc 2280 ttaaaatcat aaacaatcac atactcatce taaaattcag ggtgcaactc..cgtttcaaat ...2340. 2359 attgtatatt gtctattta

<210> 2455 DNA

Homo Sapiens

<400> cgggggagcg cggcgcggcc gccgcgtgcg cgagccgggg ttgcagccca gccgggactt 60 tccagccggc ggcagccgcg gcggtcgtcg gctcttc&cc gccccccgtc atggggcagc 120 ccggggagca gaacgctgcg gaccgcggcg gaggacgcgc\ccggcgcccc tgagccggcc 180 240 gagcggcgac ggaccgcgag aactcctctt tcctaaaatg gagtcgagta aaaagatgga ctctcctggc gcgctgcaga ctaacccgcc gctaaagctg cacactgacc gtagtgctgg 300 gacgccagtt tttgtccctg aacaaggagg ttacaaggaa aagtttgtga agaccgtgga 360 ggacaagtac aagtgtgaga agtgccacct ggtgctgtgc agcccgaagc agaccgagtg 420 480 tgggcaccgc ttctgcgaga gctgcatggc ggccctgctg agctcttcaa gtccaaaatg tacagcgtgt caagagagca tcgttaaaga taaggtgttt aaggataatt gċţgcaagag 540 agaaattotg gotottoaga totattgtog gaatgaaago agaggttgtg cagagcagtt 600 aacgctggga catctgctgg tgcatttaaa aaatgattgc cattttgaag aacttckatg 660 tgtgcgtcct gactgcaaag aaaaggtctt gaggaaagac ctgcgagacc acgtggagàa 720 ggcgtgtaaa taccgggaag ccacatgcag ccactgcaag agtcaggttc cgatgatcgc 780 gctgcagaaa cacgaagaca ccgactgtcc ctgcgtggtg gtgtcctgcc ctcacaagtg 840 cagegtecag actetectga ggagegagtt gagtgeacae ttgteagagt gtgteaatge 9,Ó 0 ccccagcacc tgtagtttta agcgctatgg ctgcgttttt caggggacaa accagcagat 960 caaggcccac gaggccagct ccgccgtgca gcacgtcaac ctgctgaagg agtggagcaa 1020

ctcgctcgaa aagaaggttt ccttgttgca gaatgaaagt gtagaaaaaa acaagagcat 1080 acaaagtttg cacaatcaga tatgtagctt tgaaattgaa attgagagac aaaaggaaat 1140 gcttcgaaat aatgaatcca\aaatccttca tttacagcga gtgatcgaca gccaagcaga 1200 gaaactgaag gagcttgaca aggagatccg gcccttccgg cagaactggg aggaagcaga 1260 cagcatgaag agcagcgtgg agtkcctcca gaaccgcgtg accgagctgg agagcgtgga 1320 caagagtgcg gggcaagtgg ctcggaacac aggcctgctg gagtcccagc tgagccggca 1380 tgaccagatg ctgagtgtgc acgacatòcg cctagccgac atggacctgc gcttccaggt 1440 cctggagacc gccagctaca atggagtgct\catctggaag attcgcgact acaagcggcg 1500 gaagcaggag gccgtcatgg ggaagaccct gtccctttac agccagcctt tctacactgg 1560 ttactttggt tataagatgt gtgccagggt cta&ctgaac ggggacggga tggggaaggg 1620 1680 gacgcacttg tcgctgtttt ttgtcatcat gcgtggagaa tatgatgccc tgcttccttg 1740 gccgtttaag cagaaagtga cactcatgct gatggatdag gggtcctctc gacgtcattt gggagatgca ttcaagcccg accccaacag cagcagcttà aagaagccca ctggagagat 1800 1860 qaatategee tetggetgee cagtetttgt ggeecaaaet gtetagaaa atgggacata 1920 tattaaagat gatacaattt ttattaaagt catagtggat achteggate tgeecgatee 1980 ctgataagta gctggggagg tggatttagc agaaggcaac tcctatgggg gatttgaacc ggtctgtctt cactgaggtc ctcgcgctca gaaaaggacc ttgtgagacg gaggaagcgg 2040 cagaaggegg acgegtgeeg gegggaggag ceaegegtga geaeacetga eaegttttat 2100 aatagactag ccacacttca ctctgaagaa ttatttatcc ttcaacaaga taaatattgc 2160 tgtcagagaa ggttttcatt ttcattttta aagatctagt taattaaggt ggaaaacata 2220 tatgctaaac aaaagaaaca tgatttttct tccttaaact tgaacaccaa aaaaaacac 2280 acacacacac acgtggggat agctggacat gtcagcatgt taagtaaaag gagaatttat 2340 gaaatagtaa tgcaattctg atatcttctt tctaaaattc aagagtgcaa ttttgtttca 2400 aatacagtat attgtctatt tttaaggcct ccaaaaaaaa aaaaaattcc ggccg 2455

```
<210> 5
```

Lys Ala Cys Lys Tyr Arg 1 5

SI,

(Jap

<211>

<212> PRT

<213> Homo Sapiens

<400> 5